# COMPENDIUM OF RELEVANT REFERENCES TO “293” & “BARIC”

Destiny Rezendes

MG77293.3

MG77293.4

FJ882933

FJ882935

FJ882934

FJ222932

FJ882936

FJ882937

FJ882939

FJ882938

229E

HK3

HEK-293 [Human Embryonic Kidney Cells]

T-293

293 common coronavirus strains

**Bat SARS-Like CoV Isolate bat-SL-CoVZC45 [Genbank: MG772933.1]**

**Institute of Military Medicine[China]- 2018 -**
**https://www.ncbi.nlm.nih.gov/nuccore/MG772933**

**D2E1F2 · D2E1F2_SARS** **https://www.uniprot.org/uniprotkb/D2E1F2/entry**

*Comparative analysis of SARS-CoV-2 and its receptor ACE2 with evolutionarily related coronaviruses* - Published online 2020 Nov 7. doi: 10.18632/aging.104024

*“We chose genome sequences of six SARS-CoV-2 strains, i.e., MT263395 (furthest), MT263421 (nearest); MT251973 (furthest), MT263420 (nearest); MT259229 (furthest), MT263389 (nearest), which were in the clades C I, C II and C III, respectively, and were the furthest or nearest from the root of the evolutionary tree. We then combined the six SARS-CoV-2 strains with 293 common coronavirus strains that infect humans in the comparative sequence analysis.”*

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7695409/

Feb 3, 2020. doi: 10.1038/s41586-020-2008-3

*A new coronavirus associated with human respiratory disease in China*

Fan Wu,#1 Su Zhao,#2 Bin Yu,#3 Yan-Mei Chen,#1 Wen Wang,#4 Zhi-Gang Song,#1 Yi Hu,#2 Zhao-Wu Tao,2 Jun-Hua Tian,3 Yuan-Yuan Pei,1 Ming-Li Yuan,2 Yu-Ling Zhang,1 Fa-Hui Dai,1 Yi Liu,1 Qi-Min Wang,1 Jiao-Jiao Zheng,1 Lin Xu,1 Edward C. Holmes,1,5 and Yong-Zhen Zhang corresponding author.

This virus strain was designated as WH-Human 1 coronavirus (WHCV) (and has also been referred to as '2019-nCoV') and its whole genome sequence (29,903 nt) has been assigned GenBank accession number MN908947. WHCV was most closely related to bat SL-CoVZC45 and bat SL-CoVZXC21, whereas in the region of nucleotides 1,030 to 1,651 (the RBD region) WHCV grouped with SARS-CoV and bat SARS-like CoVs (WIV1 and RsSHC014) that are capable of direct human transmission. Notably, WHCV is most closely related to bat coronaviruses, and shows 100% amino acid similarity to bat SL-CoVZC45 in the nsp7 and E proteins. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7094943/

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*Development of animal models against emerging coronaviruses: From SARS to MERS coronavirus:* Troy C. Sutton, Kanta Subbarao n Laboratory of Infectious Disease, NIAID, NIH, United States 22 December 2014

https://www.ctsaonehealthalliance.org/sites/default/files/documents/1-s2.0-S0042682215000768-main.pdf

To develop additional mouse-adapted virus strains, the Urbani strain was similarly passaged 20 or 25 times in two separate studies to yield lethal virus strains termed MA20 and Strain v2163 (Frieman et al., 2012; Day et al., 2009). In a direct comparison with MA15, infection with Strain v2163 resulted in significantly higher pulmonary virus titers and enhanced mortality at lower doses. Ten amino acid changes in v2163 were associated with adaptation and 4 mutations arose in the S protein. More specifically, Y436H and a second mutation at Y442F were identified in the RBD

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16 August 2010-10 Feb 2011: *Inhibition of severe acute respiratory syndrome coronavirus replication in a lethal SARS-CoV BALB/c mouse model by stinging nettle lectin, Urtica dioica agglutinin.* Yohichi Kumaki a , Miles K. Wandersee a , Aaron J. Smith a , Yanchen Zhou b,c , Graham Simmons b,c , Nathan M. Nelson a , Kevin W. Bailey a , Zachary G. Vest a , Joseph K.-K. Li d , Paul Kay-Sheung Chan e , Donald F. Smee a , Dale L. Barnard

https://static1.squarespace.com/static/5324bf63e4b05fc1fc6ea99d/t/5e831def10428029aca4c962/1585651186143/1-s2.0-S0166354211000313-main.pdf

"Because of the positive results obtained from in vitro assays and the initial studies showing the efficacy of UDA treatment in significantly reducing mortality in the lethal SARS-CoV mouse model, UDA was further evaluated in the lethal mouse model for SARS-CoV to see if efficacy could be improved. We optimized the dosage regimen to increase the effectiveness of UDA against SARS- CoV in **BALB/c mouse model in terms of survival.** We also further investigated the mode of action of UDA in vitro.

2. Materials and methods

**2.1. Cells**

Vero 76 cells, which were obtained from American Type Culture Collection (ATCC, Manassas, VA), were routinely grown in minimal essential medium (MEM) supplemented with 10% heat-inactivate fetal bovine serum (FBS, Thermo Fisher Scientific Co., Logan, UT). For in vitro antiviral assays, the serum was reduced to 2% in Vero 76 cells and gentamicin was added to the medium at a final concentration of 50 g/ml. The human primary **embryonic kidney cells (293T),** which express ACE2 **(293T-ACE2),** were obtained from the ATCC, and were cultured in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% heat-inactivated FBS.

**2.2. Viruses**

SARS-CoV, strain Urbani (200300592), was obtained from the Centers for Disease Control (CDC, Atlanta, GA, USA). The Frankfurt strain was kindly provided by Jindrich Cinatl (Klinikum der J.W. Goethe Universitat, Frankfurt Am Main, Germany). **The Toronto- 2 strain was supplied by Heinz Feldman (National Microbiology Laboratory, Winnipeg, Manitoba, Canada).** The CHUK-W1 strain was received from Paul K.S. Chan (The Chinese University of Hong Kong, China). All strains were propagated and titrated in Vero 76

cells. Personnel entering the facility wore powered air-purifying respirators (3M HEPA Air-Mate; 3M, Saint Paul, MN) and full body protection Tyvek suits."

https://static1.squarespace.com/static/5324bf63e4b05fc1fc6ea99d/t/5e831def10428029aca4c962/1585651186143/1-s2.0-S0166354211000313-main.pdf

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Craig W. Day; Ralph Baric; Sui Xiong Cai; **Matt Frieman;** Yohichi Kumaki; John D. Morrey; Donald F. Smee; Dale L. Barnard (2009). *A new mouse-adapted strain of SARS-CoV as a lethal model for evaluating antiviral agents in vitro and in vivo.* , 395(2), 210–222. doi:10.1016/j.virol.2009.09.023 || 16 September 2009

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https://core.ac.uk/download/pdf/345195433.pdf

***The Current and Future State of Vaccines, Antivirals and Gene Therapies Against Emerging Coronaviruses.*** Longping V. Tse1, Rita M. Meganck2, **Rachel L. Graham1 and Ralph S. Baric**

**Received: 11 November 2019 | Accepted: 23 March 2020 | Published: 24 April 2020**

Citation: *Tse LV, Meganck RM, Graham RL and Baric RS (2020) The Current and Future State of Vaccines, Antivirals and Gene Therapies Against Emerging Coronaviruses.* | Front. Microbiol. 11:658. doi: 10.3389/fmicb.2020.00658

Edited by: Lu Lu, **Fudan University, China**

"Cathepsin-L inhibitors MDL28170 and SSAA09E1 block SARS-CoV pseudotyped **particle infection in pre-treated 293T cells (**Simmons et al., 2005; Adedeji et al., 2013)" "). **Remdesivir has sub-micromolar inhibition concentrations in a broad range of CoVs including SARS-CoV, MERS-CoV, and hCoV-NL63, as well as pre-pandemic bat-CoVs WIV1 and SHC014 in an in vitro human airway epithelial (HAE) model** (Sheahan et al., 2017; Agostini et al., 2018). Prophylactic administration (one day pre-infection) of remdesivir can mitigate disease by reducing the viral titer and lung pathology in lethal mouse models challenged with a mouse adapted SARS- CoV MA15. **Remdesivir also shows therapeutic activity when administered early at one day post-infection** (corresponding to 7–10 days after the onset of symptoms in human infection). ***However, treatment initiated two days post infection does not improve disease outcomes,*** although the murine disease model is more compressed than in humans (Sheahan et al., 2017)"

*"...improvement of clinical outcomes on NHPs (de Wit et al., 2020).* ***The parental nucleoside of remdesivir, GS-441524, has also shown to be effective for treating FIP, a*** *disease caused by the α-CoV FIPV (Murphy et al., 2018; Pedersen et al., 2019). Currently, NHC and remdesivir are the only broadly effective antiviral drugs against all SARS-like, MERS-like, human contemporary, and animal CoVs (Sheahan et al., 2017; Agostini et al., 2018; Murphy et al., 2018; Pedersen et al., 2019).* ***Some antiviral drugs, such as chloroquine and T-705, also show efficacy in vitro and are under consideration for the current COVID-19 outbreak*** *(Wang et al., 2020)." Tse LV, Meganck RM, Graham RL and Baric RS (2020) The Current and Future State of Vaccines, Antivirals and Gene Therapies Against Emerging Coronaviruses.* Front. Microbiol. 11:658. doi: 10.3389/fmicb.2020.00658

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## Notes:

-Duke NUS Singapore was tasked to lead on the bat vaccine trials in Wuhan.

-The DEFUSE draft stated that Danielle, "will lead the animal studies."

- 2019, Danielle Anderson worked at the Wuhan Institute of Virology [WIV].

-By November 2019, Danielle left her position at the WIV without reason

-Danielle's significance/contribution to the DEFUSE project w/DARPA remains unknown.

-Jan 10, 2020, her superior, Dr. Linfa Wang [Duke NUS, Singapore] departed from his position as the Duke NUS's Emerging Infectious Disease director.

Citation* https://jimhaslam.substack.com/p/sars2-was-in-a-unc-freezer-back-in

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"The term **"293" in the context of SARS-CoV-2 refers to a comparative sequence analysis that combined six SARS-CoV-2 strains with 293 common coronavirus strains that infect humans. The analysis revealed that the 293 common coronaviruses could be divided into three clades, with 12 common coronaviruses being particularly close to the SARS-CoV-2 strains.** Interestingly, the disease caused by these 12 common coronaviruses was exclusively respiratory syndrome, and **they were identified in 2013, 2014, and 2015. The term "293" does not represent a specific group of SARS or SARS-like coronaviruses, but rather the number of common coronavirus strains used in the comparative sequence analysis."**

https://inference-review.com/article/thunder-out-of-china ^

https://doi.org/10.37282/991819.22.13

"Early sequencing aligned SARS- CoV-2 with the previously detected **RaBtCoV/4991,13,20** which was then further sequenced to give the full genome reported as **RaTG1395– defining SARS-CoV-2 as being a probable bat- origin zoonotic coronavirus.** Severe acute respiratory syndrome coronavirus (SARS-CoV), which emerged in 2002, and Middle East respiratory syndrome coronavirus (MERS-CoV), which emerged in 2012, are also considered to be of bat origin. At least 2 other commonly circulating coronaviruses in humans also likely originated in bats: HCoV-229E and HCoV-NL63."

https://www.ingentaconnect.com/contentone/aalas/cm/2021/00000071/00000005/art00010?crawler=true&mimetype=application/pdf